

We claim:

1. An isolated polypeptide having from about 50 to 79 amino acids taken from the sequence of SEQ ID NO. 1, wherein the polypeptide binds to the extracellular domain ECD of HER-2 at an affinity of at least  $10^8$ .
2. The isolated polypeptide of claim 1, wherein the isolated polypeptide is from about 69 to 79 amino acids in length.
3. The isolated polypeptide of claim 1, wherein the isolated polypeptide binds to a site on the ECD of HER-2 that is different from the site of binding of Herceptin (a marketed humanized monoclonal antibody that is used for the treatment of cancer and that binds to the ECD of HER-2).
4. An isolated DNA sequence that codes on expression for a polypeptide having from about 50 to 79 amino acids taken from the sequence of SEQ ID NO. 1, wherein the polypeptide binds to the extracellular domain ECD of HER-2 at an affinity of at least  $10^8$ .
5. The isolated DNA sequence that codes on expression for a polypeptide of claim 4 wherein the isolated polypeptide is from about 69 to 79 amino acids in length.
6. The isolated DNA sequence of claim 4, wherein the isolated polypeptide binds to a site on the ECD of HER-2 that is different from the site of binding of Herceptin®.
7. A transfected cell comprising an expression vector having a DNA sequence that codes on expression for a polypeptide having from about 50 to 79 amino acids taken from the sequence of SEQ ID NO. 1, wherein the polypeptide binds to the extracellular domain ECD of HER-2 at an affinity of at least  $10^8$ .
8. An isolated and glycosylated polypeptide having from about 300 to 419 amino acids taken from the sequence of SEQ ID NO. 2, wherein the C-terminal 79 amino acids are present, and wherein at least three N-linked glycosylation sites are present.
9. The isolated and glycosylated polypeptide of claim 6, wherein the isolated polypeptide is from about 350 to 419 amino acids in length and four N-linked glycosylation are present.
10. The isolated and glycosylated polypeptide of claim 6, wherein the isolated polypeptide binds to a site on the ECD of HER-2 that is different from the site of binding of Herceptin®.
11. An isolated DNA sequence that codes on expression for a polypeptide having from about 800 to 419 amino acids taken from the sequence of SEQ ID NO. 2, wherein the C terminal 79 amino acids are present, and wherein at least three N-linked glycosylation sites are present.
12. The isolated DNA sequence that codes on expression for a polypeptide of claim 11, wherein the isolated polypeptide is from about 350 to 419 amino acids in length and four N-

linked glycosylation sites are present.

13. A transfected cell comprising an expression vector having a DNA sequence that codes on expression for a polypeptide having from about 80 to 419 amino acids taken from the sequence of SEQ ID NO. 2, wherein the C terminal 79 amino acids are present, and wherein at least three N-linked glycosylation sites are present.

14. A method for treating a solid tumor characterized by overexpression of HER-2, comprising administering an agent that binds to the extracellular domain (ECD) of HER-2, wherein the agent is selected from the group consisting of (a) an isolated polypeptide having from about 50 to 79 amino acids taken from the sequence of SEQ ID NO. 1, wherein the polypeptide binds to the extracellular domain ECD of HER-2 at an affinity of at least  $10^8$ , (b) an isolated and glycosylated polypeptide having from about 80 to 419 amino acids taken from the sequence of SEQ ID NO. 2, wherein the C terminal 79 amino acids are present, and wherein at least three N-linked glycosylation sites are present, (c) a monoclonal antibody that binds to the ECD of HER-2, and (d) combinations thereof, with the proviso that the agent cannot be the monoclonal antibody alone.

15. The method of claim 14, wherein the solid tumor that overexpresses HER-2 is selected from the group consisting of breast cancer, small cell lung carcinoma, ovarian cancer and colon cancer.

16. The method of claim 14, wherein the agent is the isolated polypeptide having from about 50 to 79 amino acids taken from the sequence of SEQ ID NO. 1.

17. The method of claim 16, wherein the agent is a combination of the isolated polypeptide having from about 50 to 79 amino acids taken from the sequence of SEQ ID NO. 1 and the monoclonal antibody that binds to the ECD of HER-2.

18. A pharmaceutical composition for treating solid tumors that overexpress HER-2, comprising an agent selected from the group consisting of (a) an isolated polypeptide having from about 50 to 79 amino acids taken from the sequence of SEQ ID NO. 1, wherein the polypeptide binds to the extracellular domain ECD of HER-2 at an affinity of at least  $10^8$ , (b) an isolated and glycosylated polypeptide having from about 80 to 419 amino acids taken from the sequence of SEQ ID NO. 2, wherein the C terminal 79 amino acids are present, and wherein at least three N-linked glycosylation sites are present, (c) a monoclonal antibody that binds to the ECD of HER-2, and (d) combinations thereof, with the proviso that the agent cannot be the monoclonal antibody alone, and pharmaceutically acceptable carrier.

19. The pharmaceutical composition for treating solid tumors that overexpress HER-2 of claim 18, wherein the agent is the isolated polypeptide having from about 50 to 79 amino acids taken from the sequence of SEQ ID NO. 1.

20. The pharmaceutical composition for treating solid tumors that overexpress HER-2

of claim 19, wherein the agent is a combination of the isolated polypeptide having from about 50 to 79 amino acids taken from the sequence of SEQ ID NO. 1 and the monoclonal antibody that binds to the ECD of HER-2.

21. A method for targeting a therapeutic agent to solid tumor tissue, wherein the solid tumor tissue is characterized by overexpression of HER-2, comprising attaching the therapeutic agent to an isolated polypeptide having from about 50 to 79 amino acids taken from the sequence of SEQ ID NO. 1, wherein the polypeptide binds to the extracellular domain ECD of HER-2 at an affinity of at least  $10^8$ .

22. The method for targeting a therapeutic agent to solid tumor tissue of claim 21, wherein the isolated polypeptide is from about 69 to 79 amino acids in length.

23. The method for targeting a therapeutic agent to solid tumor tissue of claim 21, wherein the isolated polypeptide binds to a site on the ECD of HER-2 that is different from the site of binding of Herceptin®.

24. A method for determining the prognosis of tumor treatment in a patient for a tumor that overexpresses HER-2, comprising: (a) obtaining a bodily fluid sample from a patient, wherein the bodily fluid is selected from the group consisting blood, serum, urine, lymph, saliva, tumor tissue, placental tissue, umbilical cord tissue, amniotic fluid, chorionic villi tissue and combinations thereof; and (b) measuring the amount of p68HER-2 expressed using an anti-p68HER-2 antibody-based assay, wherein the assay is selected from the group consisting of ELISA, immunoprecipitation, immunohistochemistry, and Western analysis.

25. The method for determining the prognosis of tumor treatment for a tumor that overexpresses HER-2 of claim 24, further comprising measuring the amount of p185HER-2 ECD in the bodily fluid.

26. The method for determining the prognosis of tumor treatment for a tumor that overexpresses HER-2 of claim 24, further comprising determining a ratio between the amount of p68HER-2 and p185HER-2, whereby the higher the p68HER-2 to p185HER-2 ratio, the better the prognosis of the patient.

27. An assay for cancer treatment, prognosis or diagnosis in a patient comprising:  
(a) obtaining a bodily fluid sample from the patient, wherein the bodily fluid is selected from the group consisting of blood, serum, urine, lymph, saliva, tumor tissue, placental tissue, umbilical cord tissue, amniotic fluid, chorionic villi tissue and combinations thereof;  
(b) determining whether an ECDIIIa variant sequence is present in the bodily fluid sample using a sequence identity assay; and  
(c) correlating the presence of the ECDIIIa variant sequence to cancer treatment and diagnosis using an historical database.

28. The diagnostic assay of claim 27, wherein the sequence identity assay is selected

from the group consisting of DNA sequencing, PCR assays, ELISA immunologic assays, immunoassays, hybridization assays, and combinations thereof.

29. The diagnostic assay of claim 27, further comprising measuring the amount of p185HER-2 ECD in the bodily fluid.

30. An assay for cancer treatment, prognosis or diagnosis in a patient comprising:

(a) obtaining a bodily fluid sample from the patient, wherein the bodily fluid is selected from the group consisting of blood, serum, urine, lymph, saliva, tumor tissue, placental tissue, umbilical cord tissue, amniotic fluid, chorionic villi tissue and combinations thereof;

(b) determining whether an amount of an p68HER-2 ECDIIIa variant is present in the bodily fluid sample using an anti-p68HER-2 antibody-based assay, wherein the assay is selected from the group consisting of ELISA, immunoprecipitation, immunohistochemistry, and Western analysis; and

(c) correlating the presence or amount of the p68HER-2 ECDIIIa variant to cancer treatment and diagnosis using an historical database.

31. The diagnostic assay of claim 30, wherein the sequence identity assay is selected from the group consisting of DNA sequencing, PCR assays, ELISA immunologic assays, hybridization assays, and combinations thereof.

32. The diagnostic assay of claim 30, further comprising measuring the amount of p185HER-2 ECD in the bodily fluid.

33. The diagnostic assay of claim 32, further comprising determining a ratio between the amount of p68HER-2 and p185HER-2 ECD.

34. An antibody specific for an ECDIIIa variant of the sequence in SEQ ID NO:1 or SEQ ID NO:2.

35. An antibody specific for p68HER-2 ECDIIIa variant 3.

36. A diagnostic kit comprising:

(a) a monoclonal antibody or antigen-binding fragment thereof that specifically binds to an ECDIIIa variant of the sequence in SEQ ID NO:1 or SEQ ID NO:2; and

(b) a detectable label, whereby the binding of the antibody in step (a) can be detected.

37. The diagnostic kit of claim 36, wherein the label is selected from the group consisting of enzymes, radiolabels, chromophores, chemiluminescent tags, and fluorscers.